REMARKS

Claims 1-22 and 64-74 were pending in the application. In the Office Action mailed December 28, 2005, claims 1-10, 12-21 and 64-74 were allowed, claims 11 and 22 were rejected. In the instant Amendment, claims 11 and 22 have been amended to clarify the invention, and claims 75-76 have been added. Upon entry of the instant response, claims 1-22 and 64-76 will be pending.

Claim 11 has been amended to clarify that both D_{target} and $D_{off-target}$ are activities of the drug against biological pathways in *a cell*, and that both D_{target} and $D_{off-target}$ are determined based on measurements of a plurality of cellular constituents *of said cell* (emphasis added). Claim 22 has been amended similarly. Support for the amendment is found in the specification at, e.g., page 7, lines 29-31; and page 11, lines 20-35.

New claims 75-76 have been added. Support for new claims 75-76 is found in the specification at page 7, lines 29-34.

No new matter is added by these amendments. Entry of the above made amendments and consideration of the following remarks are respectfully requested.

THE REJECTION UNDER 35 U.S.C. § 102 (b) and (e) SHOULD BE WITHDRAWN

Claims 11 and 22 are rejected under 35 U.S.C. § 102 (b) and (e) as being anticipated by Goldenberg, U.S. Patent No. 5,332,567 ("Goldenberg"). The Examiner contends that Goldenberg teaches a variety of different measurements of binding of a drug to target sites vs. non-target sites to produce a ratio of target to non-target localization, and thus, Goldenberg anticipates claim 11 and 22 of the present application. Applicants respectfully disagree with the Examiner for reasons set forth below.

A claim is anticipated under 35 U.S.C. § 102 only if each and every element and limitation as set forth in the claim is found, either expressly described or inherently present, in a single prior art reference. *Glaxo, Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047 (Fed. Cir. 1995). There must be *no differences* between the claimed invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991). Inherent

anticipation may not be established by probabilities or possibilities. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991), quoting *In re Oelrich*, 666 F.2d 578 (CCPA 1981).

At the outset, Applicants respectfully submit that the rejected claims have been amended to clarify that, in the claimed methods, both D_{target} and $D_{\text{off}-\text{target}}$ are activities of the drug against biological pathways in *a cell*, and that both D_{target} and $D_{\text{off}-\text{target}}$ are determined based on measurements of a plurality of cellular constituents *of said cell* (emphasis added). The rejected claims (as amended) relate to a method for evaluating specificity of a drug comprising comparing activity of a drug against its target pathway (D_{target}) in a cell and activity of said drug against at least one of its off-target pathways ($D_{\text{off}-\text{target}}$) in the cell. In the claimed methods, D_{target} and $D_{\text{off}-\text{target}}$ are each determined based on measurements of a plurality of cellular constituents of the cell. The comparing step comprises calculating a specificity index (SI) according to the formula:

$$\text{SI} = \frac{n \bullet D_{\text{target}}}{\sum D_{\text{off}-\text{target}}}$$

wherein n is the number of off-target pathways. In the present invention, a biological pathway in a cell refers to a collection of cellular constituents in a cell related in that each cellular constituent of the collection is influenced according to some biological mechanism by one or more other cellular constituents in the collection (see, e.g., the specification at page 7, lines 16-30).

In contrast, Goldenberg teaches a method of targeting a diagnostic or therapeutic agent to a location of infection by injecting a patient infected with a pathogen parenterally with an antibody conjugate which specifically binds to an accessible epitope of the pathogen or a pathogen-associated antigen accreted at the location of infection (Goldenberg, Abstract). The antibody conjugate comprises a bound diagnostic or therapeutic agent for detecting, imaging or treating the infection. Goldenberg teaches that by using an antibody conjugated with a diagnostic or therapeutic, the diagnostic or therapeutic is localized at the target site with an enhanced target to non-target ratio. Goldenberg teaches that the localization of the antibody conjugate can be assayed by various detection methods. Thus, in Goldenberg, it is a pathogen or a pathogen-associated antigen in the body of a patient that is detected, and the

detected binding of the antibody conjugate to the pathogen or pathogen-associated antigen is compared with detected binding of the antibody conjugate to non-target that is anything in the patient to which the antibody conjugate may bind other than the target pathogen or pathogen-associated antigen.

Thus, Applicants respectfully submit that Goldenberg does not teach the methods of the rejected claims. Firstly, Goldenberg does not teach determining the activities of a target pathway and a non-target pathway in *the same cell* by use of measurements of cellular constituents of *that same cell*, as is now specified by the amended claims. Instead, Goldenberg teaches detecting its antibody conjugate in a mammal by imaging after injection of the antibody conjugate into the mammal (see, e.g., Goldenberg at col. 13, line 18 through col. 14, line 10). Goldenberg teaches determining a ratio of its antibody conjugate on different sites in the body of a mammal, i.e., a site of infection versus other sites (see, e.g., Goldenberg at col. 3, lines 41-58), not determining activities on different pathways of the same cell by measuring cellular constituents of that cell. While Goldenberg teaches that its target and non-target are in the body of the same patient, Goldenberg does not teach that its target and non-target are "constituents" of the same cell. Thus, the ratio of Goldenberg is not a ratio of activity against a target pathway and activity against at least one off-target pathway in a cell.

Nor does Goldenberg inherently teach the methods of the rejected claims, because Goldenberg's teachings do not necessarily result in the practice of the claimed invention. The court held in *Continental Can Co. v. Monsanto Co.* that

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient. [Citations omitted.]

Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1269 (Fed. Cir. 1991), quoting *In re Oelrich*, 666 F.2d 578 (CCPA 1981). Not only does Goldenberg not disclose localization of its antibody conjugate to target and off-target sites of the same cell, the methods taught by Goldenberg would not even be expected to permit such a result, since the imaging taught by Goldenberg is not done at the level of individual cells.

Thus, Applicants respectfully submit that Goldenberg does not teach expressly or inherently determining the specificity of a drug by comparing activities of the drug against different biological pathways in a cell, i.e., by comparing activity of the drug against its target

pathway (D_{target}) in a cell and activity of the drug against at least one off-target pathway ($D_{off-target}$) in that cell, wherein each of D_{target} and $D_{off-target}$ are based on measurements of a plurality of cellular constituents of that cell. As such, Goldenberg does not anticipate claims 11 and 22, as amended, and the rejection of these claims under 35 U.S.C. § 102 (b) and (e) based on Goldenberg should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections and allowance of the application are respectfully requested.

Respectfully submitted,

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